

Response to Office Action of February 24, 2003
Application No. 09/715,418

IN THE SPECIFICATION

Please amend the specification as follows:

On page 5, the paragraph at lines 20-21, please amend to read as follows:

Figure 1 is a ClustalW alignment of the carboxy 104 amino acids of the human polypeptide of SEQ ID NO:6 with known S100 cytokine proteins.

On page 5, the paragraphs from line 26 to page 6, line 11, please amend to read as follows:

Figure 3 is a Pfam analysis of human EST AA315020 (~~SEQ ID NO:4~~) (SEQ ID NO:38).

Figure 4A is a BLOCKS protein domain analysis of the polypeptide of SEQ ID NO:6 with other calcium binding proteins (SEQ ID NOs:12-36).

Figure 4B shows an alignment of amino acids 28-131 of SEQ ID NO:3 with amino acids 1-101 of Acc. No. AY007220 (SEQ ID NO:39), an S-100 type calcium binding protein, and the resulting consensus sequence (SEQ ID NO:40).

Figure 4C shows an alignment of amino acids ~~28-131~~ 15-118 of SEQ ID NO:6 with amino acids 1-101 of Acc. No. AY007220 (SEQ ID NO:39); the consensus sequence is shown as SEQ ID NO:40.

Figure 4D shows an alignment of a region of the polypeptide of SEQ ID NO:3 with various calcium binding domains (SEQ ID NOs:41-44); the consensus sequence derived from the alignment is shown as SEQ ID NO:45.

Figure 4E shows an alignment of a region of the polypeptide of SEQ ID NO:6 with various previously described calcium binding domains (SEQ ID NOs:41, 42, 44 and 46); the consensus derived from the alignment is shown as SEQ ID NO:47.

On page 6, the paragraph at lines 19-20, please amend to read as follows:

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Figure 7 is a CAP alignment and consensus of human assembly 65677221-3-frag (SEQ ID NO:5) compared to human EST AA315020 (SEQ ID NO:49; the complementary strand sequence of SEQ ID NO:4) and CuraGen assembly 65677221.

On page 9, the paragraph at lines 16-20, please amend to read as follows:

The polypeptides whose sequences are shown in Table 3 and Table 6 have a high degree of similarity with the S100 family of proteins. FIG. 1 demonstrates this similarity for the human sequence shown in Table 6. The sequence identified as "W27152" in Fig. 1 (SEQ ID NO:10) is disclosed as a "chemotactic cytokine II CCII polypeptide" in PCT publication WO97/34013, and the polypeptide designated "G491246" (SEQ ID NO:11) is a Macrophage Migration Inhibition Factor (MRP-14).

On page 9, the paragraph at lines 28-30, please amend to read as follows:

Moreover, analysis by the BLOCKS program (see Fig. 4A) shows the two conserved calcium binding regions separated by about 8 amino acids, which is a characteristic of S100 proteins (Kligman, 1988 Trends Biochem. Sci. 13:437). Sequences shown in Figure 4A are identified in Table 11.

Please insert Table 11 immediately following the amended paragraph at page 9, lines 28-30.

Table 11

SEQ ID NO:	Molecule	SEQ ID NO:	Molecule
12	3-100/ICaBP type calcium binding protein	25	Glypicans protein
13	3-100/ICaBP type calcium binding protein	26	Membrane attack complex component/perforin
14	Bacterial type II secretion system protein F	27	Urease nickel ligands protein
15	Ubiquitin carboxyl-terminal hydrolases family	28	Phosphoglycerate mutase family phosphohistidine
16	Bacterial chemotaxis sensory	29	Ribosomal protein L23 protein

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	transducers protein		
17	Phosphoenolpyruvate carboxykinase (ATP) protein	30	2'-5'-oligoadenylate synthetase protein
18	Prokaryotic-type carbonic anhydrases protein	31	Formate and nitrite transporter protein
19	Ergosterol biosynthesis ERG4/ERG24 family protein	32	Glycoprotein hormones β chain protein
20	Lysosome-associated membrane glycoproteins duplicated domains protein	33	Vinculin family talin-binding region protein
21	Phosphofructokinase proteins	34	β -lactamase class B protein
22	pH domain proteins profile	35	Heat shock hsp20 protein family profile
23	Myotoxins protein	36	Hydroxymethylglutaryl- coenzyme A lyase protein
24	Phosphatidylinositol-specific phospholipase X		

On page 10, the paragraphs at lines 1-13, please amend to read as follows:

Figs-Figures 4B-4E show comparisons of portions of the amino acid sequences shown in Table 3 (SEQ ID NO:3) and Table 6 (SEQ ID NO:6) to S-100-type calcium binding proteins. Fig-Figure 4B shows an alignment of amino acids 28-131 of SEQ ID NO:3 with amino acids 1-101 of Acc. No. AYY007220 (SEQ ID NO:39), a calcium binding protein. Identical or conserved amino acid residues are indicated in black shading. These residues may be required to preserve structural or functional properties of the protein. Amino acids shaded in gray can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function, e.g., L to V, I or M. Non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function. The consensus sequence is shown in SEQ ID NO:40.

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~~Fig.~~Figure 4C shows an alignment of amino acids ~~28-131~~ 15-118 of SEQ ID NO:6 with amino acids 1-101 of Acc. No. AY007220 (SEQ ID NO:39).

~~Fig.~~Figures 4B and 4C demonstrate that the polypeptides shown in Tables 3 and 6 included extensive regions identical or conserved with the amino acid sequence of Acc. No. AY007220 (SEQ ID NO:39); amino acids 15-118 of SEQ ID NO:6 are shown in Figures 4B and 4C; the consensus sequence derived from these alignments is given as SEQ ID NO:40.

On page 10, the paragraph at lines 20-22, please amend to read as follows:

~~Fig.~~Figure 4D shows an alignment of a region of the polypeptide of Table 3 (amino acids 46 to 85 of SEQ ID NO:3) with various calcium binding domains (SEQ ID NOs:41 (gi/4139958/pdb/1MHO), 42 (Protein MRP-126), 43 (ICTACALCIN) and 44 (CALGRANULIN B). The consensus sequence is given in SEQ ID NO:45. Fig. 4E shows an alignment of a region of the polypeptide of Table 6 (amino acids 33 to 72 of SEQ ID NO:6) with various previously described calcium binding domains (SEQ ID NOs:41 (gi/4139958/pdb/1MHO), 42 (Protein MRP-126), 44 (CALGRANULIN B and 46 (CALGRANULIN B). The consensus sequence is given in SEQ ID NO:47.

On page 88, the paragraph at line 23 to page 89, line 2, please amend to read as follows:

This process was used to assemble the sequence of SEQ ID NO:5 encompassing the sequence of SEQ ID NO:4 (shown as the complementary strand, SEQ ID NO:49), including providing base calls for the two unidentified bases in SEQ ID NO:4. Three separate SeqCalling fragments were identified in this search (shown as assembly 65677221+ (SEQ ID NO:37)), two arising from embryonic tumor cell lines (CuraGen Nos. 61097801 and 61124196), and one from endothelial cells (primary dermal endothelial cell from Cell Application, San Diego, CA; CuraGen No. 60920173) that were treated with the cytokines IL-1beta (2ng/ml) and TNF-alpha (5ng/ml) for 16hrs in order to induce leukocyte adherence. The alignment of the resulting assembly with the original EST AA315020 (SEQ ID NO:4) to provide the consensus sequence identified as SEQ ID NO:5 is shown in Fig. 7. This consensus was obtained using the CAP alignment program (Huang X, Genomics 1992 Sep;14(1):18-25).